

### REMARKS/ARGUMENTS

Claims 1-12 and 19-20 are active. Claims 13-18 have been withdrawn from consideration. New Claims 19-20 have been added. Claim 1 has been amended to require that the pH-sensitive polymer not contain transition metals. Such polymers are disclosed and exemplified by the present specification (see, e.g., Table 1 on page 25 of the specification) and do not raise the issue of new matter, see MPEP 2163.07(a). Similarly, new Claims 19-20 find support in pH-sensitive polymers exemplified in the specification, as well as on page 14 of the specification which discloses particular polymerization methods, including the GTP and ATRP methods. Accordingly, the Applicants do not believe that any new matter has been added.

### Restriction/Election

Applicants previously elected with traverse, Group I, Claims 1-12, directed to a pH-sensitive polymer and a method of making it. New Claims 19-20 are directed to pH-sensitive polymers and should be properly grouped with elected Group I. Claims 13-18, directed to medicinal substances containing the pH-sensitive polymer, have been withdrawn from consideration. The Restriction Requirement has now been made FINAL.

The Applicants respectfully request that the claims of the nonelected group which depend from or include all the limitations of those of elected Group I, be rejoined upon an indication of allowability for the elected claims, see MPEP 821.04.

### Rejection—35 U.S.C. §102 or §103

Claims 1-11 were rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative under 35 U.S.C. 103(a) as being obvious over, Haddleton et al., U.S. Patent 5,804,632. Haddleton does not disclose or suggest the invention of the present invention,

since the Haddleton polymers contain toxic transition metal ions, such as cobalt, which remain from the catalytic chain transfer (CCT) polymerization which requires the presence of these toxic metals, see Haddleton, col. 1, lines 50-52 and col. 3, lines 34-40.

Furthermore, these remaining transition metals are toxic and thus would not bring about less than 5% hemolysis at pH 7.4 as required by Claim 1, because they would kill cells exposed to them. Accordingly, Haddleton does not anticipate the present invention and does not render it obvious, since there is no disclosure or suggestion of polymers not containing toxic transition metals, nor of complexes which bring about less than 5% hemolysis at pH 7.4. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §103

Claim 12 was rejected under 35 U.S.C. 103(a) as being unpatentable over Haddleton et al., U.S. Patent 5,804,632 as applied to Claims 1-11 above, and further in view of Rehmer et al., U.S. Patent No. 6,225,401. Haddleton does not disclose or suggest the invention for the reasons discussed above. Rehmer was cited as teaching the element of a polymerization regulator. However, it does not disclose or suggest pH-sensitive polymer of the invention. Accordingly, this rejection may now be withdrawn.

Rejections—35 U.S.C. §102 or §103

Claims 1-11 were rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative under 35 U.S.C. 103(a) as being obvious over, Lehmann et al., U.S. Patent 5,705,189. Lehmann does not disclose or suggest the pH-sensitive polymers of the invention for the following reasons.

Lehmann discloses polymers having molecular weights ranging from 50,000 to 1,500,000 daltons (col. 3, line 40) and does not suggest selecting polymers having a

molecular mass of 50,000 daltons or less as required by Claim 1. Polymers having such high molecular masses can accumulate in the body because their excretion by glomerular filtration is prevented, see the specification, page 6, lines 1-16 and page 8, lines 1-12. However, Lehmann is unconcerned with this, since the Lehmann polymers are intended for coatings and binders for pharmaceutical agents and not for introducing biomolecules or drugs into cellular cytoplasm.

Furthermore, Lehmann does not disclose or suggest selecting polymers which bring about at least 60% haemolysis at pH 5.5 and less than 5% haemolysis at pH 7.4. These properties permit the pH-sensitive polymers to efficiently deliver biomolecules and drugs into a cell (specification, page 5, lines 30 ff.).

The Official Action assumes that these properties are inherent to the genus of polymers disclosed by Lehmann, however, as shown in Table 4 of the specification (page 29), polymers falling within the genus broadly described by Lehman do not have these functional properties. For example, polymer S-100 (composition shown in Table 1, page 25) falls within the compositional ranges disclosed by Lehmann, but does not inherently have the property of inducing at least 60% haemolysis at pH 5.5. Therefore, the Applicants have demonstrated that the broad genus of polymers described by Lehmann do not inherently have the functional properties required by the present invention.

Moreover, Lehmann provides no motivation to select polymers having these particular functional properties and a molecular mass of 50,000 daltons or less, or provide a reasonable expectation of success for obtaining pH-sensitive polymers having these desirable properties by making such a selection.

Thus, the Applicants respectfully request that this rejection be withdrawn because Lehmann does not disclose, suggest or provide a reasonable expectation of success for

obtaining the polymers having the molecular weight and physiological properties of the pH-sensitive polymers of the invention.

#### Rejection—35 U.S.C. §103

Claim 12 was rejected under 35 U.S.C. 103(a) as being obvious over Lehmann et al., U.S. Patent 5,705,189 as applied to Claims 1-11 above, and further in view of Rehmer et al., U.S. Patent No. 6,225,401. Lehman and Rehmer alone or in combination do not disclose or suggest the present invention for the reasons discussed above.

#### Rejections—35 U.S.C. §102 or §103

Claims 1-11 were rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative under 35 U.S.C. 103(a) as being obvious over, Lehmann et al., U.S. Patent 5,644,011. Lehmann does not disclose or suggest the pH-sensitive polymers of the invention for the following reasons.

Lehmann discloses polymers having molecular weights ranging from 50,000 to 3,000,000 daltons (col. 3, line 65) and does not suggest selecting polymers having a molecular mass of 50,000 daltons or less as required by Claim 1. As discussed above, polymers having such high molecular masses can accumulate in the body because their excretion by glomerular filtration is prevented, see the specification, page 6, lines 1-16 and page 8, lines 1-12. However, Lehmann is unconcerned with this, since the Lehmann polymers are intended for coatings and binders for pharmaceutical agents and not for introducing biomolecules or drugs into cellular cytoplasm (see Lehmann's Abstract).

Furthermore, Lehmann does not disclose or suggest selecting polymers which bring about at least 60% haemolysis at pH 5.5 and less than 5% haemolysis at pH 7.4. These

properties permit the pH-sensitive polymers to efficiently deliver biomolecules and drugs into a cell (specification, page 5, lines 30 ff.).

The Official Action assumes that these properties are inherent to the genus of polymers disclosed by Lehmann, however, as shown in Table 4 of the specification (page 29), polymers falling within the genus broadly described by Lehman do not have these functional properties. For example, polymer S-100 (composition shown in Table 1, page 25) falls within the compositional ranges disclosed by Lehmann, but does not inherently have the property of inducing at least 60% haemolysis at pH 5.5. Therefore, the Applicants have demonstrated that the broad genus of polymers described by Lehmann do not inherently have the functional properties required by the present invention.

Moreover, Lehmann provides no motivation to select polymers having these particular functional properties and a molecular mass of 50,000 daltons or less, or provide a reasonable expectation of success for obtaining pH-sensitive polymers having these desirable properties by making such a selection.

Thus, the Applicants respectfully request that this rejection be withdrawn because Lehmann does not disclose, suggest or provide a reasonable expectation of success for obtaining the polymers having the molecular weight and physiological properties of the pH-sensitive polymers of the invention.

#### Rejections—35 U.S.C. §103

Claim 12 was rejected under 35 U.S.C. 103(a) as being obvious over, Lehmann et al., U.S. Patent 5,644,011 as applied to Claims 1-11 above, and further in view of Rehmer et al., U.S. Patent No. 6,225,401. Lehman and Rehmer alone or in combination do not disclose or suggest the present invention for the reasons discussed above.

CONCLUSION

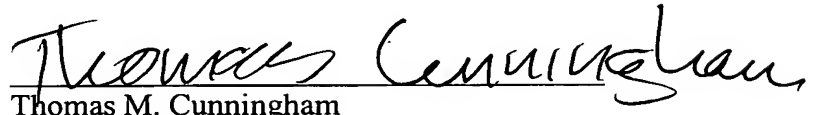
In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. An early notification to that effect is earnestly solicited.

Respectfully submitted,

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